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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,096	06/15/2000	David J. Diller	1073.060	8927

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EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	28

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/595,096

Applicant(s)

DILLER ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/14/03 has been entered.

All rejections and objections not reiterated below are hereby withdrawn.

Information Disclosure Statement

The IDS filed 3/14/03 has been considered in full.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-10 are directed to a computer-implemented method of docking a ligand into a binding site of a protein which comprises a variety of mathematical steps. It is noted that the claims recite ONLY steps of mathematical manipulation of data.

According to MPEP 2106.IV.B.1:

"If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

- consist solely of mathematical operations without some claimed practical application

(i.e., executing a "mathematical algorithm"); or

- simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application.

Cf. Alappat, 33 F.3d at 1543 n.19, 31 USPQ2d at 1556 n.19..."

The MPEP, at 2106, also states that claims may be statutory where the claimed invention as a whole, accomplishes a practical application. "That is, it must produce a "useful, concrete and tangible result." State Street, 149 F.3d at 1373, 47 USPQ2d at 1601-02." The claims do not recite a "result" of any kind such that the claimed method steps accomplish a practical application. The claims do not recite identification of particular ligands, or a particular binding site. In fact, the claims do not recite any particular protein for use in the method. As claims 1-10 recite only

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mathematical manipulations of data and do not recite any "practical application" or any "result" which may be considered "useful, concrete and tangible," the claims are not directed to statutory subject matter.

Claims 11-20 are directed to a "computer-aided system" comprising "means" for performing various acts, wherein the acts appear to be those of mathematical manipulation. No physical or "hardware" limitations are recited in claims 11-20, therefore it does not appear that the claimed "system" is a physical product, but is merely a listing of computer-implemented steps; i.e. a computer program. A computer program, per se, is not statutory subject matter. As set forth in MPEP 2106 IV.B.1 (a): "Similarly, computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical "things." They are neither computer components nor statutory processes, as they are not "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory."

It is noted that claims 21-30, directed to computer-readable medium comprising a program, is directed to statutory subject matter, and is not rejected herein. MPEP 2106 IV.B.2 (b) states:

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"If a claim defines a useful machine or manufacture by identifying the physical structure of the machine or manufacture in terms of its hardware or hardware and software combination, it defines a statutory product. See, e.g., Lowry, 32 F.3d at 1583, 32 USPQ2d at 1034-35; Warmerdam, 33 F.3d at 1361-62, 31 USPQ2d at 1760.

Office personnel must treat each claim as a whole. The mere fact that a hardware element is recited in a claim does not necessarily limit the claim to a specific machine or manufacture. Cf. *In re Iwahashi*, 888 F.2d 1370, 1374-75, 12 USPQ2d 1908, 1911-12 (Fed. Cir. 1989), cited with approval in *Alappat*, 33 F.3d at 1544 n.24, 31 USPQ2d at 1558 n.24."

Claims 11-20 do not recite any physical, structural, or "hardware" limitations defining the "system" as a machine or product of manufacture, therefore claims 11-20 are not directed to statutory subject matter.

Claims 1-30 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claims are directed to a method, and a "system" and program for performing the method, for docking a ligand to a protein. The claims do not recite any steps of identifying ligands, any particular proteins to which a ligand is docked, or any other "result" of the method, as set forth above. The specification discloses, on page 3, that the "ultimate goal" of the inventive method is to use molecular docking to prioritize combinatorial library screening efforts; i.e. to rank entire libraries instead of individual compounds. An *in silico* method to screen libraries of compounds for a particular

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activity (e.g. inhibition/activation of a protein with known activity) would have a patentable utility. However, as set forth above, the instant claims do not recite any particular protein for which ligand binding/docking is evaluated. The claims do not recite any selection, screening, identification, etc. steps for any set of ligands docked to a protein. It is possible to use docking methods to identify or design receptors for known ligands. A method of identifying or designing a receptor for a ligand with a known function (utility) would also have utility under 35 USC 101. However, the claims do not recite any particular ligands, and do not recite any steps of identification or design of either a ligand or a receptor.

The Court of Customs and Patent Appeals has stated:

"Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." A "use" to do further research is not considered a utility which provides an "immediate benefit" to the public. Examples of situations requiring further research to identify or reasonably confirm a "real world" context of use, and which do not have utility under 35 USC 101, as set forth in MPEP 2107.01.I, include:

- (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
- and
- (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility.

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As neither a ligand or protein with known utility is recited in the claims, and the claims do not recite any steps which result in an "immediate benefit" to the public, the claims do not have utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11, and 21 recite "performing" a conformational search "to generate" multiple conformations of a ligand. Searching is not generally considered by those skilled in the art to be synonymous with generating. One may search for conformations of a molecule, and one may generate a library or grouping of conformations found/identified by the search (as in claims 2, 12, and 22), or one may search a variety of conformations previously generated (as in claims 4, 14, and 24 where clustering and retaining "top numbers" of clusters follows a generation step), but one does not usually generate conformations *with* a search. As it is unclear what steps applicant actually intends, the claims are indefinite.

Claims 2, 12, and 21 limit the searching steps of claims 1, 11, and 21, respectively, to comprise "creating a database of the multiple conformations of the

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ligand” It is unclear if the step of creating a database is intended to precede the step of “generating” multiple conformations of the ligand of the parent claim, replaces the generation step, or follows the generation step, therefore claims 2, 12, and 21 are indefinite.

Claims 4, 14, and 24 limit the searching steps of parent claims 1, 11, and 21 to comprise a step of randomly generating a plurality of conformations (of the ligand). However, the parent claims recite a step of performing a search to generate multiple conformations of a ligand. It is unclear if the generation step of claims 4, 14, and 24 is intended to replace the generation step of the parent claim, or be an additional generation step, therefore claims 4, 14, and 24 are indefinite.

Claims 1, 11, and 21 recite computer-implemented steps/means of performing a conformational search to generate multiple conformations of a ligand “in solution.” Similarly, claims 2-3, 12-13, and 22-23 recite a “database” of multiple conformations of a ligand “in solution.” Claims 7, 17, and 27 recite matching atoms of “the ligand in solution” to hot spots of a protein. It is unclear whether applicant intends to generate/match actual solution-based conformations of the ligand (e.g. a physical step), or intends all of the steps, and database, to be computer-implemented, therefore the claims are indefinite. Neither the originally filed specification or claims provide support for a step of physically generating multiple conformations of a ligand in solution. The specification, on page 4, and the original claims recited generation of “solution conformations” of a ligand. Given the context of the phrase on the specification and original claims, the examiner interprets “solution conformations” to mean virtual, or

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computer-generated, conformations which correlate to conformations available for a ligand were it in solution phase. This is not support for a physical step. Applicant states on page 10 of the response filed 3/14/03 that the phrase "in solution" was used, in part, to clarify applicant's invention. Unfortunately, addition of this phrase rendered the claims indefinite for the reasons set forth above. As it does not appear that applicant intended a physical method step, the claims are not rejected herein for new matter, but only for indefiniteness.

Claim 4 recites "the molecule" in line 3. Claim 7 recites "the molecule" in line 7. There is no antecedent basis for "the molecule" in the claims, therefore the claims are indefinite. As parent claim 1 recites a "ligand," this rejection may be overcome by replacing "molecule" with --ligand--, if such is consistent with applicant's intent.

Conclusion

Claims 1-30 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

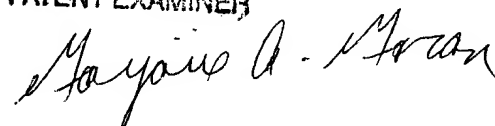
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

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308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

A handwritten signature in cursive script, reading "Marjorie A. Moran", written in dark ink.

mam
June 12, 2003